

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

40136

CHEMISTRY REVIEW(S)

AND A APPROVAL SUMMARY

ANDA: 40-136 FIRM: Luitpold
DRUG PRODUCT: Hydralazine Hydrochloride Injection USP
DOSAGE FORM: injection STRENGTH: 20 mg/mL

CGMP STATEMENT/EIR UPDATE STATUS: Acceptable on 03-11-97

BIO STUDY: Waiver granted on 06-13-97

VALIDATION: Satisfactory per memo dated 06-07-96 (no analytical problems encountered, however, product did not meet USP spec for pH, firm has provided 12 months of shelf life data to support the expiration date, data provided supports this)

STABILITY: Glass vials with coated teflon stoppers are used in the test batch and also same on stability.

Expiration Date: 12 months; based on 3 months accelerated data and 12 months of shelf life

Specifications:

LABELING: satisfactory on 07-05-96

STERILIZATION VALIDATION: [

] APPROVAL, 04-07-97

SIZE OF BIOBATCH: DMF [] 06-05-97 - ADEQUATE

SIZE OF STABILITY BATCHES: [] L

PROPOSED PRODUCTION BATCH: [] L The manufacturing process is the same as that used for the stability batch.

CHEMIST: /S/ 6-16-97
TEAM LEADER:

1. CHEMISTRY REVIEW NO. 3 2. ANDA # 40-136
3. NAME AND ADDRESS OF APPLICANT
Luitpold Pharmaceuticals, Inc
Att: Robert Anderson, B.A., J.D.
One Luitpold Drive, Shirley, NY 11967
4. LEGAL BASIS FOR SUBMISSION Apresoline® HCl from Ciba-Geigy,
no patents on file and no exclusivity
5. SUPPLEMENTS N/A 6. PROPRIETARY NAME N/A
7. NONPROPRIETARY NAME Hydralazine Hydrochloride Injection, USP
8. SUPPLEMENTS PROVIDE FOR: N/A
10. PHARMACOLOGICAL CATEGORY 11. Rx
antihypertensive, used in emergency situations when the drug
cannot be given orally
12. RELATED IND/NDA/DMF(s) N/A
13. DOSAGE FORM sterile solution for IM or IV administration;
packaged as a 1 ml fill in 2 ml single dose glass vials
14. POTENCY 20 mg/ml
15. CHEMICAL NAME AND STRUCTURE
1-hydrazinophthalazine monohydrochloride, C₈H₈N₄ · HCl
M.W.=196.94, CAS [304-20-1]
16. RECORDS AND REPORTS N/A
17. COMMENTS See comments in **bold** throughout the review.
18. CONCLUSIONS AND RECOMMENDATIONS **APPROVE**
19. REVIEWER: Melissa Maust DATE COMPLETED: June 16, 1997

cc: ANDA 40-136
Division File

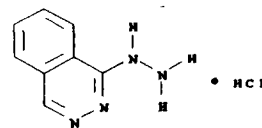
Endorsements:

HFD-623/M. Maust/ **/S/**
HFD-623/V. Sayeed, Ph.D./

6-16-97

/S/

6/17/97



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Chem Review # 3

2. ANDA # 40-136

3. NAME AND ADDRESS OF APPLICANT

Luitpold Pharmaceuticals, Inc
Attention: Ms. Audrey Bialeski
One Luitpold Drive, Shirley, NY 11967

4. LEGAL BASIS FOR SUBMISSION Apresoline® HCl from Ciba-Geigy,
no patents on file and no exclusivity

5. SUPPLEMENTS N/A

6. PROPRIETARY NAME N/A

7. NONPROPRIETARY NAME Hydralazine Hydrochloride Injection, USP

8. SUPPLEMENTS PROVIDE FOR: N/A

9. AMENDMENTS AND OTHER DATES:

Original Submission	02-17-95
Refusal to file letter	04-05-95
Amendment	05-10-95
Refusal to file letter	06-01-95
Amendment	10-04-95
Acceptable for filing	10-05-95
Acknowledgement to firm	10-25-95
Deficiency Letter	04-18-96 +
CMC Major Amendment	06-21-96 -this review
Labeling Review-SATIS	07-05-96
Micro Review-DEFICIENT	08-08-96

10. PHARMACOLOGICAL CATEGORY

11. Rx

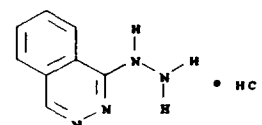
antihypertensive, used in emergency situations when the drug cannot be given orally

13. DOSAGE FORM sterile solution for IM or IV administration;
packaged as a 1 ml fill in 2 ml single dose glass vials

14. POTENCY 20 mcg/ml

15. CHEMICAL NAME AND STRUCTURE

1-hydrazinophthalazine monohydrochloride, $C_8H_8N_4 \cdot HCl$
M.W.=196.94, CAS [304-20-1]



17. COMMENTS : See deficiencies in **bold** throughout the review.

18. CONCLUSIONS AND RECOMMENDATIONS NA/MINOR

19. REVIEWER: Melissa Maust DATE COMPLETED: October 31, 1996
Revised: November 13, 1996

cc: ANDA 40-136
Division File

Endorsements:

HFD-623/M. Maust
HFD-623/V. Sayeed, Ph.D. /

11-13-96

• 11/15/96

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Chem Review # 2

1. CHEMISTRY REVIEW NO. 1 2. ANDA # 40-136
3. NAME AND ADDRESS OF APPLICANT
Luitpold Pharmaceuticals, Inc
One Luitpold Drive, Shirley, NY 11967
516-924-4000
4. LEGAL BASIS FOR SUBMISSION Apresoline Hydrochloride from
Ciba-Geigy, no patents on file and no exclusivity
5. SUPPLEMENTS N/A
6. PROPRIETARY NAME N/A
7. NONPROPRIETARY NAME Hydralazine Hydrochloride Injection, USP
8. SUPPLEMENTS PROVIDE FOR: N/A

9. AMENDMENTS AND OTHER DATES:
- | | |
|-------------------------|----------|
| Original Submission | 2/17/95 |
| Refusal to file letter | 4/5/95 |
| Amendment | 5/10/95 |
| Refusal to file letter | 6/1/95 |
| Amendment | 10/4/95 |
| Acceptable for filing | 10/5/95 |
| Acknowledgement to firm | 10/25/95 |

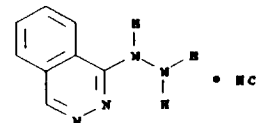
10. PHARMACOLOGICAL CATEGORY NSAID 11. Rx

13. DOSAGE FORM sterile solution for intramuscular or
intravenous administration; packaged as a 1 ml fill in 2 ml
single dose glass vials

14. POTENCY 20 mg/ml

15. CHEMICAL NAME AND STRUCTURE

Hydralazine Hydrochloride, USP
1-hydrazinophthalazine monohydrochloride, $C_8H_8N_4 \cdot HCl$
M.W.=196.94, CAS [304-20-1]



17. COMMENTS See deficiencies in **bold** throughout the review.

18. CONCLUSIONS AND RECOMMENDATIONS NA/MAJOR

19. REVIEWER: Melissa Maust DATE COMPLETED: February 9, 1996
revised: February 26, 1996

cc: ANDA 40-136
Division File

Endorsements:

HFD-623/M. Maust, /S/ 2/24/96
HFD-623/A. Rudman, Ph.D. /S/ - 2/23/96

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